

## Outcome and preferences in male-to-female subjects with gender dysphoria: Experience from Eastern India

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### ABSTRACT

**Context:** Gender dysphoria (GD) is an increasingly recognized medical condition in India, and little scientific data on treatment outcomes are available. **Aims:** Our objective is to study the therapeutic options including psychotherapy, hormone, and surgical treatments used for alleviating GD in male-to-female (MTF) transgender subjects in Eastern India. **Subjects and Methods:** This is a retrospective study of treatment preferences and outcome in 55 MTF transgender subjects who were presented to the endocrine clinic. **Statistical Analysis Used:** Descriptive statistical analysis is carried out in the present study, and Microsoft Word and Excel are used to generate graphs and tables. **Results:** The mean follow-up was 1.9 years and 14 subjects (25.5%) were lost to follow-up after a single or 2–3 contact sessions. Rest 41 subjects (74.5%) desiring treatment had regular counseling and medical monitoring. All 41 subjects were dressing to present herself as female and all of them were receiving cross-sex hormone therapy either estrogen only (68%), or drospirenone in combination with estrogen (12%) or gonadotropin-releasing hormone agonist (GnRH) in combination with estrogens (19.5%). Most of the subjects preferred estrogen therapy as it was most affordable and only a small number of subjects preferred drospirenone or GnRH agonist because of cost and availability. 23.6% subjects underwent esthetic breast augmentation surgery and 25.5% underwent orchiectomy and/or vaginoplasty. Three subjects presented with prior breast augmentation surgery and nine subjects presented with prior orchiectomy without vaginoplasty, depicting a high prevalence of poorly supervised surgeries. **Conclusions:** Standards of care documents provide clinical guidance for health professionals about the optimal management of transsexual people. The lack of information among health professionals about proper and protocolwise management leads to suboptimal physical, social, and sexual results.

**Key words:** Eastern India, gender dysphoria, gender identity disorder, hormone and surgical treatments, male-to-female transsexuals

### INTRODUCTION

Gender identity disorder according to the International Classification of Diseases 10<sup>th</sup> revision<sup>[1]</sup> is a desire to live and be accepted as a member of the opposite sex, usually accompanied by a sense of discomfort with, or

inappropriateness of one's own anatomic sex and a wish to have hormonal treatment and surgery to make one's body as congruent as possible with the preferred sex. Affected individuals are commonly referred to as transgender. The transsexual identity must not be a symptom of another mental disorder, such as schizophrenia or associated with any intersex, genetic or sex chromosome abnormality. In May 2013, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) has replaced this category with "Gender Dysphoria" (GD).<sup>[2]</sup> Sex assignment

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or gender assignment is the determination of an infant's sex at birth by a relative, nurse, or physician after inspecting the genitalia when the baby is delivered. Female-to-male denotes to assigned female persons who identify oneself as male, and male-to-female (MTF) refers to assigned male persons who identify oneself as female.<sup>[3]</sup> Over the past decade, there has been an increase in the number of transgender or gender variant people seeking care because of many reasons. They have greater access to information through the Internet, have more exposure to transgender characters in the media and the nationwide publicity of the Supreme Court judgment on the transgender issue. The landmark decision by the Supreme Court of India on April 15, 2014, declared transgender people to be a "third gender," affirmed that the fundamental rights granted under the Constitution of India will be equally applicable to transgender people and gave them the right to self-identification of their gender as male, female, or third gender.<sup>[4]</sup> In this study, we retrospectively evaluated the outcome of MTF GD subjects treated in the endocrine clinic of the KPC Medical College, Kolkata, India.

## SUBJECTS AND METHODS

The reference population comprised MTF transgender subjects attending a single endocrine referral center in Kolkata between April 2010 and November 2015. The hospital is a low-cost health institute serving low socioeconomic groups. The endocrine clinic of the KPC Medical College and Hospital offers comprehensive hormonal management for the transgender persons in close association with psychiatry department of the hospital. Most of the transgender got operated in their preferred institute and continued follow-up in our clinic. We have included all subjects receiving consultation and care from the clinic and excluded the subjects recently (<6 months) enrolled, for analysis.

GD is a condition where the person identifies himself with the opposite of their original biological sex. Diagnosis of GD is thus important to rule out other concurrent or underlying mental disorders (anxiety, depression, etc.), and GD must be separated from transvestism, homosexuality, or concurrent congenital intersex condition. A multidisciplinary team is required, and a detailed psychiatric history, psychosexual development, and behavior history are required for the diagnosis. In our center, a three-member team comprising two Endocrinologists and one Psychiatrist is involved in the process of confirming the diagnosis based on the DSM-5.<sup>[2]</sup> According to the DSM-5, for a person to be diagnosed with GD, there must be a marked difference between the individual's expressed/experienced gender and his assigned (natal) gender, and it must continue for at least

6 months. The condition must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

This is a retrospective and cross-sectional outcome study of MTF GD subjects. The protocol was presented to the hospital Ethics Committee who felt that given the retrospective nature of the study, informed consent could be dispensed with. Demographic data collected include age at the time of baseline visit. Most of our patients return for follow-up approximately every 3 months. However, there was a wide range of timing of follow-up visits. Only subjects with a baseline and at least 3 follow-up visits were included in the study.

The descriptive statistical analysis is carried out in the present study. Results of continuous measurements are presented as mean  $\pm$  standard deviation, and results of categorical measurements are presented in number (%). Microsoft Word and Excel are used to generate graphs and tables.

## RESULTS

Retrospective and cross-sectional outcome of 55 MTF GD subjects is analyzed. The baseline demographic and descriptive characteristics of the subjects are outlined in Table 1.

All of the 55 MTF transgender subjects were evaluated by the mental health professionals (MHPs) to confirm the diagnosis and were also counseled by the MHPs. Fourteen of them (25.5%) were lost to follow-up after a single or 2–3 contact sessions (<6 months) before cross-sex hormone therapy. Rest of all 41 subjects (74.5%) were dressing to present herself as female (Real Life Experience or RLE) from the beginning. They were followed for a mean 1.9 years in the endocrine clinic [Table 1]. Cross-sex hormone therapy was offered to all subjects who were eligible for cross-sex hormone treatment as per laid down guidelines.<sup>[5]</sup> Eight subjects were already receiving some oral contraceptive pills without any medical supervision in an attempt to impart some feminizing character, and at the time of analysis, all 41 subjects were receiving feminizing hormone therapy. Three already had had esthetic breast augmentation surgery without going through the protocol-wise approach before presenting to our center, and another ten subjects (total 13, 23.6%) completed the same as per the standard of care. Nine subjects already had had orchiectomy without vaginoplasty (6 by the persons who dishonestly pretended to have medical skills and 3 by medically qualified surgeons) before presenting to our center and another five subjects (total 14, 25.5%) underwent

**Table 1: Baseline characteristics of the study sample**

Parameters and treatment modalities	Subject (%)
Number of subjects ( <i>n</i> )	55 (100)
Age at presentation (years), mean±SD	25.77±6.25
Lost to follow-up	14 (25.5)
Duration of treatment, mean (years)	1.9
Psychiatry counseling	55 (100)
RLE	41 (74.5)
Cross-sex hormone therapy	41 (74.5)
Breast surgery	13 (23.6)
Orchiectomy and/or vaginoplasty	14 (25.5)

SD: Standard deviation, RLE: Real life experience

**Table 2: Preferences of hormone therapy in male to female transgender**

Hormone therapy	Estrogen only (%)	Drospirenone + estrogen (%)	GnRH + estrogen (%)
41	28 (68)	5 (12)	8 (19.5)

GnRH: Gonadotropin-releasing hormone

orchiectomy and vaginoplasty as per the standard of care [Table 1].

The hormone regimens for MTF transgender subjects are complex and they were treated with three different regimens: with estrogen only, with drospirenone (progestin with anti-androgen activity) in combination with estrogen or with gonadotropin-releasing hormone agonist (GnRH agonist) in combination with estrogen, depending on the response and affordability. The majority (68%) were managed with estrogen. Only 12% received drospirenone in combination with estrogen and 19.5% received GnRH agonist in combination with estrogen [Table 2].

## DISCUSSION

GD is a difficult disorder to deal with and difficult in counseling the patient about the range of treatment options and their implications. The family members want to “cure” their “patient,” while on the other hand, the GD person battles with a myriad of emotions and seeks help to make sense of the situation.<sup>[6]</sup> The goal is not to change how the person feels about his or her gender. Instead, the goal is to deal with the distress that may come with those feelings. In India, a transsexual individual is often an outcast and no specific guidelines for the management of transsexualism exist. Our current treatment approach for MTF transgender individuals was based on the Endocrine Society Clinical Practice guideline<sup>[5]</sup> and the Standards of Care from the World Professional Association for Transgender Health.<sup>[7]</sup>

The focus of the medical encounters was to bring the physical appearance more in-line with the internal gender identity of the individual and this was achieved through four stages. First, MHPs accurately diagnosed the GD,

counseled about the range of treatment options, their implications, and limitations of reassignment surgery and engaged the subject in psychotherapy. Second, the RLE is to test the capacity to function in the gender with which they identify themselves. A documented RLE for at least 3 months was a requirement before prescribing hormone therapy and sex reassignment surgery (SRS).<sup>[7]</sup> Third, cross-sex hormone therapy was prescribed to induce development of female sex characteristics and to decrease the physical characteristics of the undesired male sex.<sup>[8]</sup> And fourth, surgery for sex reassignment which includes breast augmentation surgery, genital surgery for removal of the gonads and vaginoplasty, who fulfilled the eligibility and readiness criteria for SRS.<sup>[5]</sup> In our experience, many subjects (27 out of 55, almost 49%) did not complete the whole treatment, and even if some of them completed (14 out of 55, almost 25%), they failed to adhere to the lifetime commitment for hormonal therapy. In most of the situations, the failure to adhere to the hormonal therapy was because of cost or side effect of the drugs. However, it is well known that often with the help of psychotherapy, some individuals do not feel the need to feminize their body, some patients may need hormones, but not surgery and many individuals may need both hormone therapy and surgery to alleviate their GD.<sup>[7]</sup>

Because GD may be accompanied with psychological or psychiatric problems, it is necessary that the diagnosis be made by an MHP who can make a distinction between GD and conditions that have similar features and can diagnose comorbid psychiatric conditions accurately, if any, associated with GD.<sup>[5]</sup> All the MTF transgender subjects had completed the initial sessions with MHPs (including those lost to follow-up). MHPs diagnosed the individual's GD, any comorbid psychiatric condition, and arranged their appropriate treatment. MHP informed the subjects about the possibilities and limitations of sex reassignment to prevent unrealistically high expectations from treatment. MHPs engaged the subjects in psychotherapy and ascertained the eligibility/readiness for hormone and surgical therapy.<sup>[7]</sup> We have observed a significant high dropout after a single or 2–3 contact sessions at endocrine clinic among MTF transgender (*n* = 14, 25.5%) and clinicians using treatments with the strongest empirical support cannot be effective if patients drop out of treatment prematurely. Many patients came in with unrealistic assumptions and expectations about the therapy, in terms of the roles of the treating physician, surgeon, and the duration of treatment. It was very disappointing for many that the benefit appeared slowly, surgery had limitations, involved high cost, required a lifetime treatment, and a high degree of commitment on the part of the patient. All these factors might be the

explanation of high dropout after a single or two contact sessions [Table 1].

The RLE was a period in which transgender individuals lived full-time in the gender with which they identify. The purpose of the RLE was to confirm that the MTF transgender person could function successfully as female gender in society, as well as tested the person's resolve and the capacity to live full-time as a female for the rest of their life. A documented RLE of at least 3 months duration is a requirement for prescribing hormone therapy and a requirement for performing SRS.<sup>[5]</sup> All 41 subjects gracefully accepted the dressing to present herself as female and lived full-time as a female [Table 1]. Some of them had an initial hesitancy to start dressing to present herself as female in known social circle. They were advised to start in an unknown social circle (during traveling or from beginning of joining a new institution, etc.) and then in family and lastly in a known social circle.

Cross-sex hormone therapy (mostly estrogen) was started once the MHP ascertained the eligibility and readiness for hormone therapy and the subject demonstrated knowledge and understanding of the expected outcomes of hormone treatment, as well as the risks.<sup>[5]</sup> Hormone therapy was individualized, based on a patient's goals, the risk/benefit ratio, the presence of other medical conditions, and economic issues.<sup>[7]</sup> MTF transgender can be effectively managed through exogenous feminizing hormone administration to induce development of female sex characteristic.<sup>[8]</sup> Previous venous thrombotic events, history of estrogen-sensitive neoplasm, and end-stage chronic liver disease are contraindications to feminizing hormone therapy.<sup>[7]</sup> Eight subjects were already receiving some oral contraceptive pills without any medical advice in a desperate attempt to change their sex. All of them were from "hizra" community.<sup>[9]</sup> "Hizras" live a ghetto-like existence, in their own communities and commonly use oral contraceptive pills among themselves.<sup>[9]</sup> In our center, most MTF transgender were effectively managed with estrogen only (68%) [Table 2]. We had used estrogen (conjugated or ethinyl estrogen) mostly as oral tablets.

Measurement of serum estradiol levels was used as a guide to therapy in all patients, and the target was to maintain the serum estradiol level at the mean daily level for premenopausal women (<200 pg/ml).<sup>[5]</sup> The electrochemiluminescence immunoassay was used to measure serum estradiol level in our hospital. Parenteral estrogen (oestradiol valerate) was used when oral tablets failed to induce expected result (breast growth, decreased erectile function, decreased testicular size, and increased in body fat) and serum estradiol level of adult biological

women not achieved. We had no experience of using transdermal estrogen.

The antiandrogens has shown to be effective to reduce endogenous testosterone levels, ideally to levels found in adult biological women, to enable estrogen therapy to have its fullest effect. Two categories of these medications are drospirenone (progestin with antiandrogen activity) and GnRH agonist.<sup>[5]</sup> Some of the MTF transgender were managed with drospirenone in combination with estrogen (12%) and others with GnRH agonist in combination with estrogen (19.5%), depending on the response. The monthly GnRH agonist (leuprolide acetate) with estrogen, was very effective in reducing testosterone levels with low incidence of adverse reactions<sup>[5]</sup> but were sparingly used ( $n = 8$ ) due to the prohibiting cost of therapy [Table 2]. Cyproterone acetate, a progestational compound with antiandrogenic properties is widely used in Europe,<sup>[10]</sup> but we have no experience with this. Flutamide blocks binding of androgens to the androgen receptor, but it does not lower serum testosterone levels, has liver toxicity and has questionable efficacy,<sup>[5]</sup> and was never used in our center. Long-term effects of cross-sex hormone treatment in MTF transgender may not be very safe and management may be complicated due to osteoporosis at the lumbar spine or distal arm and thromboembolic and/or other cardiovascular events.<sup>[11]</sup>

For the MTF transgender, surgical procedures included the breast surgery (augmentation mammoplasty) and genital surgery (penectomy, orchiectomy, vaginoplasty, clitoroplasty, vulvoplasty).<sup>[7]</sup> Surgery was recommended when the patient fulfilled the eligibility and readiness criteria laid down in guideline and who were receiving cross-sex hormones responsibly during the last 12 months and had a successful continuous full-time RLE during the last 12 months.<sup>[5]</sup> Breast augmentation surgery was delayed until at least 2 years of estrogen therapy had been completed, given that the breasts continue to grow during that time with estrogen stimulation.<sup>[5]</sup> Three subjects already had esthetic breast augmentation surgery without going through the protocol-wise approach before presenting to our center. It highlights the lack of information among the health care providers about the protocol and standard of care for the transgender population. Totally, 13 subjects (23.6%) had completed the esthetic breast augmentation surgery [Table 1].

Many MTF transgender choose to join the "hizra" community of their own free will, and many of them undergo crude and yet radical removal of external genitalia by the persons who dishonestly pretended to have medical skills.<sup>[9]</sup> SRS may be the necessary last step toward achieving

the ultimate goal of living successfully in the desired gender role among some but not all MTF transgender. Nine subjects had orchiectomy without vaginoplasty before presenting to our center, six by some unqualified persons who dishonestly pretended to have medical skills and surprisingly three, by medically qualified surgeons. These people are far too quick to the knife and irreversible surgeries, rather than helping patients deal with the deeper issues of their dysphoria, and this may lead to suboptimal physical, social, and sexual results.<sup>[9]</sup> We are yet to plan for genital reconstructive surgery for these nine poorly managed subjects with mutilating surgery. Another five subjects (total = 14, 25.5%) were managed with planned genital surgery as per standard of care [Table 1].

Changing transgender people's birth name and sex in the official gazette and official identity documents either after realizing their gender identity or undergoing SRS is a challenge in India.<sup>[6]</sup> The recent landmark Judgment by Supreme Court of India has identified transgender people as the third gender<sup>[4]</sup> and they may identify themselves as the third gender in voter card and passport. However, there is a long way to go before people with GD are freed from the stigma.

## CONCLUSIONS

GD is an increasingly recognized medical condition in India. Published guidelines<sup>[5,7]</sup> provide clinical guidance about the optimal management with safe and effective pathways, and GD can in large part be alleviated through treatment. Lack of information and awareness among many health personnel often leads to risky procedures and inappropriate handling of people seeking transition. A transsexual individual is often an outcast and a country specific guideline is a distant reality in India. The whole issue

is complicated by the ambiguous and often discriminatory law,<sup>[6]</sup> and we have a long way to go to resolve these issues.

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## Conflicts of interest

There are no conflicts of interest.

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